REMARKS

Claims 104-108, 121, 123, 127-144 and 155 are now pending in this application.

The pending claims have been amended and new claim 155 has been added to more particularly point out and distinctly claim the invention.

Claims 109-120, 122, 124-126 and 145-154 have been canceled without prejudice or disclaimer. The amendments to the claims and the addition of new claim 155 are fully supported within the originally filed application such as within originally pending now canceled claims 1-82 with specific reference being made to original claims 1 and 3-7.

No new matter has been added.

Response to Restriction Requirement

In response to the Restriction Requirement applicants **elect Group IX** containing claims 104-106, 121, 123, 125-135 and 142 with traverse and request the claims of Groups X and XIX be examined along with the elected group.

Applicants respectfully request that the Examiner reconsider the Restriction Requirement and specifically reconsider examining all of the claims now pending within the application.

Amended claim 104 is directed to a non-human monoclonal antibody or portion thereof which is reactive to human, mouse and rat connective tissue growth factors. This monoclonal antibody could be produced by different hybridoma such as the hybridoma specifically referred to within claim 105 of the elected group as well as claim 107 which is contained within non-elected Group X.

Further, the claimed monoclonal antibody could be used in a method as claimed within dependent claims 136-141 which claims have been placed within the non-elected Group XIX.

Applicants recognize that by combining Groups IX, X and XIX that art cited against the claims of Group IX involving hybridoma FERM BP-6208 may also be citable against claims of Group X, including hybridoma FERM BP-6209 or claims of Group XIX involving hybridoma FERM BP-6208 or hybridoma FERM BP-6209.

Even with consideration to the traversal of the Restriction Requirement as described above applicants have made considerable concessions in response to the Restriction Requirement by the cancellation of a significant number of claims and via amendments such as the significant amendment made to independent claim 104. Forcing applicants to prosecute 23 different applications would be

unduly burdensome in view of the scope of the invention. Accordingly, in view of the above applicants respectfully request reconsideration of the Restriction Requirement and examination of all of the claims now pending within the application.

LEGAL BASIS FOR TRAVERSAL

The present application was filed under Rule 371. Accordingly, the PCT rules regarding "unity of invention" apply. The test for "single inventive concept" or "unity of invention" is as follows: do the claims share one or more "special technical features." The expression "special technical features" is defined in PCT Rule 13.2 and refers to those technical features that define a contribution which each of the inventions, considered as a whole, makes over the prior art.

The rationale for the restriction is that Groups I-XXIII do not relate to a single general inventive concept because Group XXI (claim 145), directed to transgenic mouse carrying a DNA encoding human CTGF, is obvious in view of the prior art and, therefore, does not share a "special technical feature" with the remaining claims. While the rationale for the Restriction may explain why claim 145 should be restricted from the remaining claims, it does not explain why restriction of the remaining claims into 22 other groups is necessary and proper.

For example, the Restriction fails to provide any reasoning as to why the alternative of claim 104 lack unity of invention (e.g. how the alternatives are not "of a similar nature," sharing "significant structural elements"). Therefore, the restriction of independent claim 104 into 10 distinct groups should be reconsidered and withdrawn.

In a similar manner the Restriction fails to explain how an independent claim (e.g. claim 104) can lack unity with one or more claims depending thereon (e.g., claim 109), a suggestion which is contradictory with the PCT Administrative Instructions. Quoting from the MPEP, "Instructions Concerning Unity of Invention" (see MPEP, Appendix A1):

> "Unity of invention has to be considered in the first place only in relation to the independent claims and not the dependent claims. If the independent claims avoid the prior art and satisfy the unity of invention, no problem of lack of unity arises in respect to any claims that are dependent on the independent claims. In particular, it does not matter if a dependent claim itself contains a

further invention."

The present Restriction Requirement fails to demonstrate that independent claim 104 both (a) does not avoid the prior art and (b) does not satisfy the unity of invention test (see above). Thus, again, as the Restriction has failed to assert this position, the restriction between independent claim 104 (Groups I-X) and dependent claims 109 *et seq.* (Groups XI-XVIII) should be reconsidered and withdrawn.

In the event any fees are due in connection with the filing of this amendment or if petitions are required, applicants petition for any required relief and authorize the Commissioner to charge the cost of such petitions or other fees to our Deposit Account No. 50-0815.

Respectfully submitted,
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Date: 19/Oct/2001

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VERSION TO SHOW CHANGES WITH MARKINGS

IN THE CLAIMS

Please **cancel** claims 109-120, 122, 124-126 and 145-154 without prejudice or disclaimer. Please amend claims 104-108, 121, 123 and 127-144 and add new claim 155 as shown on the attached "Mark-Up Version of the Claims." A clean copy of the amended and added claims appear below.

104. (Once Amended) A non-human monoclonal antibody or a portion thereof, [comprising a property selected from the group consisting:

(a)] which is reactive to human, mouse and rat connective tissue growth factors (CTGFs)[;

(b) reactive to both human and mouse CTGFs but not reactive to rat CTGF;

(c) reactive to both mouse and rat CTGFs but not reactive to human CTGF;

(d) reactive to rat CTGF;

(e) inhibiting binding of human CTGF to human kidney-derived fibroblast cell line 293-T (ATCC CRL1573), or the binding of mouse CTGF to said cell line 293-T;

(f) inhibiting binding of human CTGF to any cells of rat kidney-derived fibroblast cell line NRK-49F (ATCC CRL-1570), human osteosarcoma-derived cell line MG-63 (ATCC CRL-1427), or human lung-derived fibroblasts;

(g) inhibiting cell proliferation of rat kidney-derived fibroblast cell line NRK-49F (ATCC CRL-1570) induced by stimulus with human or mouse CTGF;

(h) inhibiting an increase of an elevated level of hydroxyproline in the kidney;

(i) obtainable by immunizing a mouse with human CTGF or a portion thereof, and reactive to human, mouse and rat CTGFs;

(j) obtainable by immunizing a hamster with mouse CTGF or a portion thereof, and reactive to human, mouse and rat CTGFs;

(k) obtainable by immunizing a rat with mouse CTGF or a portion thereof, and reactive to human, mouse and rat CTGFs;

(l) obtainable by immunizing a mouse with human CTGF or a portion thereof, reactive to human, mouse and rat CTGFs and inhibiting binding of human CTGF to human kidney-derived

fibroblast cell line 293-T (ATCC CRL1573);

(m) obtainable by immunizing a rat with mouse CTGF or a portion thereof, reactive to human, mouse and rat CTGFs and inhibiting binding of mouse CTGF to human kidney-derived fibroblast cell line 293-T (ATCC CRL1573); and,

(n) obtainable by immunizing a hamster with mouse CTGF or a portion thereof, and reactive to human, mouse and rat CTGFs and inhibiting binding of mouse CTGF to human kidney-derived fibroblast cell line 293-T (ATCC CRL1573)].

105. (Once Amended) The non-human monoclonal antibody or a portion thereof according to claim 104, wherein said monoclonal antibody is produced by a hybridoma identified by [an] international deposit accession No. FERM BP-6208.

106. (Once Amended) The non-human monoclonal antibody or a portion thereof according to claim 104, wherein said monoclonal antibody comprises a property substantially equivalent to that of a monoclonal antibody produced by a hybridoma identified by [an] international deposit accession No. FERM BP-6208.

107. (Once Amended) The non-human monoclonal antibody or a portion thereof according to claim 104, wherein said monoclonal antibody is produced by a hybridoma identified by [an] international deposit accession No. FERM BP-6209.

108. (Once Amended) The non-human monoclonal antibody or a portion thereof according to claim 104, wherein said monoclonal antibody comprises a property substantially equivalent to that of a monoclonal antibody produced by a hybridoma identified by [an] international deposit accession No. FERM BP-6209.

Please cancel claims 109-120

121. (Once Amended) A cell producing the non-human monoclonal antibody according to claim 104.

Please cancel claim 122.

123. (Once Amended) The cell according to claim 121, wherein said cell is a hybridoma obtainable by fusing a mammalian myeloma cell with a mammalian B cell which is capable of producing the non-human monoclonal antibody.

Please cancel claims 124-126.

127. (Once Amended) [A] The cell according to claim 121, wherein said cell is a hybridoma identified by [an] international deposit accession numbers selected from the group consisting of [FERM BP-6535, FERM BP-6598, FERM BP-6599, FERM BP-6600,] FERM BP-6208 and FERM BP-6209.

128. (Once Amended) An antibody-immobilized insoluble carrier on which the non-human monoclonal antibody according to claim 104 is immobilized.

129. (Once Amended) The non-human antibody-immobilized insoluble carrier according to claim 128, wherein said insoluble carrier is selected from the group consisting of plates, test tubes, tubes, beads, balls, filters and membranes.

130. (Once Amended) The non-human antibody-immobilized insoluble carrier according to claim 128, wherein said insoluble carrier is a filter or membrane, or that used for affinity column chromatography.

131. (Once Amended) A labeled antibody which is prepared by labeling the non-human monoclonal antibody or a portion thereof according to claim 104 with a labeling agent capable of providing a detectable signal by itself or together with other substances.

132. (Once Amended) The labeled non-human antibody according to claim 131, wherein said labeling agent is an enzyme, fluorescent substance, chemiluminescent substance, biotin, avidin, or radioisotope.

133. (Once Amended) A kit for detecting or assaying mammalian CTGF, comprising the non-human monoclonal antibody or a portion thereof according to claim 104.

134. (Once Amended) A kit for detecting or assaying mammalian CTGF comprising an antibody-immobilized insoluble carrier on which the non-human monoclonal antibody according to claim 104 is immobilized.

135. (Once Amended) A kit for detecting or assaying mammalian CTGF comprising a labeled antibody which is prepared by labeling the non-human monoclonal antibody or a portion thereof according to claim 104 with a labeling agent capable of providing a detectable signal by itself or together with other substances.

136. (Once Amended) A method for detecting or assaying mammalian CTGF by an immunoassay, comprising at least the following steps of (a) and (b):

(a) reacting a sample with an antibody-immobilized insoluble carrier on which the non-human monoclonal antibody according to claim 104 is immobilized; and,

(b) reacting a labeled antibody which is prepared by labeling the monoclonal antibody or a portion thereof according to claim 104 with a labeling agent capable of providing a detectable signal by itself or together with other substances, with an antigen-antibody complex formed by binding mammalian CTGF in said sample to the antibody-immobilized insoluble carrier.

137. (Once Amended) A method for detecting or assaying mammalian CTGF by an immunoassay, comprising at least the following steps of (a) and (b):

(a) reacting a sample with a labeled antibody which is prepared by labeling the monoclonal antibody or a portion thereof according to claim 104 with a labeling agent capable of providing a detectable signal by itself or together with other substances; and,

(b) reacting an antibody-immobilized insoluble carrier on which the monoclonal antibody according to claim 104 is immobilized, with the antigen-antibody complex formed by binding said labeled antibody and mammalian CTGF in said sample.

138. (Once Amended) A method for detecting or assaying mammalian CTGF by an immunoassay, comprising at least the following step of (a):

(a) reacting a mixture comprising an antibody-immobilized insoluble carrier on which the monoclonal antibody according to claim 104 is immobilized, a labeled antibody which is prepared by labeling the monoclonal antibody or a portion thereof according to claim 104 with a labeling agent capable of providing a detectable signal by itself or together with other substances, and a sample.

139. (Once Amended) A method for detecting or assaying mammalian CTGF by an immunoassay, comprising at least the following step of (a):

(a) reacting a sample and a mammalian CTGF standard labeled with a labeling agent capable of providing a detectable signal by itself or together with other substances, with an antibody-immobilized insoluble carrier on which the non-human monoclonal antibody according to claim 104 is immobilized.

140. (Once Amended) A method for detecting or assaying mammalian CTGFs by an immunoassay, comprising at least the following steps of (a) and (b):

(a) reacting the non-human monoclonal antibody or a portion thereof according to claim 104 with a mixture comprising a sample and a mammalian CTGF standard labeled with a labeling agent capable of proving a detectable signal by itself or together with other substances; and,

(b) reacting a mammalian antiserum reactive to said monoclonal antibody with the antigen-antibody complex formed by binding mammalian CTGF in said sample or said labeled mammalian CTGF standard and said monoclonal antibody.

141. (Once Amended) A method for detecting or assaying mammalian CTGFs by an immunoassay, comprising at least the following steps of any of (a) to (c):

(a) reacting the non-human monoclonal antibody or a portion thereof according to claim 104 with a sample;

(b) reacting a mammalian CTGF standard labeled with a labeling agent capable of providing a detectable signal by itself or together with other substances with a reaction product resulted from the reaction in step (a); and,

(c) reacting a mammalian antiserum reactive to said monoclonal antibody with the antigen-antibody complex formed by binding mammalian CTGF in said sample or said labeled mammalian CTGF standard, and said monoclonal antibody.

142. (Once Amended) A kit for separating or purifying mammalian CTGF, comprising an antibody-immobilized insoluble carrier on which the non-human monoclonal antibody according to claim 104 is immobilized.

143. (Once Amended) A method for separating or purifying mammalian CTGF, comprising using affinity chromatography with an antibody-immobilized insoluble carrier on which the non-human monoclonal antibody according to claim 104 is immobilized.

144. (Once Amended) The [purification method for] method for separating or purifying mammalian CTGF according to claim 143, wherein said affinity chromatography is affinity column chromatography.

Please cancel claims 145-154.

Please add the following new claim 155.

155. (New) The non-human monoclonal antibody or a portion thereof according to claim 104, said non-human monoclonal antibody characterized by inhibiting the binding of human CTGF to human kidney-derived fibroblast cell line 293-T (ATCC CRL1573).